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The Ability of the Brain to Adapt to Temporal Lobe Epilepsy in the Context of Hemispheric Dominance for Language

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THE ABILITY OF THE BRAIN TO ADAPT TO TEMPORAL LOBE EPILEPSY IN THE CONTEXT OF HEMISPHERIC DOMINANCE FOR LANGUAGE

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Dissertation Approval

This is to certify that the thesis presented to us by ________________________________

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Committee Members' Signatures:

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Abstract

The potential for the brain to adapt to insult or injury is demonstrated in the preservation of language functions when there is damage to the language areas (Lidzba, Staudt, Wilke, Grodd, & Krageloh-Mann, 2006). Although atypical hemispheric dominance for language is rare in the general population, rates are higher in epilepsy patients (Araujo, Schwarze, & White, 2009; Drane et al., 2012; Lidzba, Staudt, Wilke, Grodd, et al., 2006; Powell, Kemp, & Garcia-Finana, 2012; Spreer et al., 2001). Understanding this relationship and factors affecting atypicality is important for neuropsychologists in making treatment recommendations and for pre-operative planning. This study sought to understand the relationship of hemispheric dominance to the crowding hypothesis, cognitive reserve theory, and patterns on neuropsychological test data. The current literature is reviewed. Archival data from an urban hospital in southeastern Pennsylvanian was used. After accounting for inclusion and exclusion criteria, 185 participants were included in this study. Hemispheric dominance for language was not related to crowding or cognitive reserve independently. The interaction between crowding and cognitive reserve was found to be related to hemispheric dominance for language, with cognitive reserve accounting for the bulk of the effect. Nevertheless, this effect vanishes when right temporal lobe epilepsy (RTLE) versus left temporal lobe epilepsy (LTLE) patients are separated into individual samples. Hemispheric dominance was not related to discrete neuropsychological profiles. Potential explanations, implications, and limitations are discussed.

Keywords: Hemispheric dominance for language, temporal lobe epilepsy, crowding hypothesis, cognitive reserve

Table of Contents

List of Tables

Chapter 1: Introduction

Statement of the Problem

The plasticity of the brain and potential for reorganization is demonstrated in the relative sparing of language functioning when there is either acute or diffuse damage to the language areas (Lidzba, Staudt, Wilke, Grodd, et al., 2006). Left hemispheric dominance for language has been found in approximately 80% to 97% of right-handed individuals, and 74% to 78% of left-handed individuals (Donaldson & Johnson, 2006; Mazoyer et al., 2014; Powel et al., 2012; Sveller et al., 2006). The temporal lobe, in particular, has been shown to play an important role in language functions (Besson et al., 2014). Furthermore, patients with temporal lobe epilepsy (TLE) have been shown to have deficits in language ability on standard neuropsychological protocols (Jensen et al., 2011). Nevertheless, language functions can be spared even when there is extensive damage to the left hemisphere (Lidzba & Stoudt, 2008; Lidzba, Staudt, Wilke, Grodd, et al., 2006). Additionally, some patients with left hemisphere lesions show relatively little impairments in their language functioning, but demonstrate impairments in other cognitive functions such as nonverbal tasks (Lidzba, Staudt, Wilke, Grodd, et al., 2006). The brain is able to compensation for insult or injury in a variety of ways (Tracy & Osipowicz, 2011) that may be contributing to this pattern.

Cognitive reserve theory is the most researched mechanism of compensation and has been used to explain how similar neuropathology can result in varying clinical outcomes. Cognitive reserve theory suggests that the disparity between the degree of brain damage and the clinical presentation is moderated by a patient's cognitive reserve (Akman, Hu, Fu, & Holmes, 2003). Therefore, the amount of cognitive reserve an individual possesses could influence the extent of crowding a patient demonstrates. Cognitive reserve theory takes into consideration the varying environmental factors that would have influenced brain growth and development, as well as the potential for future recovery. Factors that influence levels of cognitive reserve include premorbid intelligence, education, and occupation (Akman et al., 2003), and have been referred to as "an intellectually enriching lifestyle" in the literature (Sumowski & Leavitt, 2013, p. 1123). Education, occupation, and intellectual stimulation are considered to be the factors that make up the enriched environment that contributes to an individual's cognitive reserve.

Cognitive reserve has been used to explain the disparity between the degree of brain pathology and clinical presentation, primarily in patients with varying forms of dementia (Akman et al., 2003). Cognitive reserve theory posits that individual differences in neuronal networks allow some patients to cope better with brain injury (Stern, 2009). Studying cognitive reserve in epilepsy patients has been difficult due to the potential for epilepsy treatment and care, IQ, education, and occupation to influence each other (Akman et al., 2003). Nevertheless, some research suggests the underlying mechanism behind cognitive reserve theory, hippocampal neurogenesis or the growth of new neurons in the hippocampus (Kempermann, Gast, & Gage, 2002; Ruan et al., 2014; Stern, 2009), can be used to explain recovery and the potential sparing of functions in epilepsy patients (Pai & Tsai, 2005). Increased hippocampal neurogenesis occurs for individuals in an enriched environment, such as for those engaging in ongoing education or mental exercises (Pai & Tsai, 2005), and has been linked to cerebral functioning in the elderly (Pai & Tsai, 2005). Cognitive reserve theory could influence the sparing of cognitive functions in individuals with temporal lobe lesions because individuals in an enriched environment may have the benefit of increased hippocampal neurogenesis leading to an increase in neuronal networks.

The crowding hypothesis is a behavioral observation of the deficit pattern seen in patients with left temporal lobe lesions. Lansdell (1969) first observed this pattern of a sparing of language functions with impairments in nonverbal functions in 1969. The crowding hypothesis was proposed by Teuber in 1974, and suggests that the resilience of language functioning comes at the expense of nonverbal functions (Strauss, Satz, & Wada, 1990). This hypothesis proposes that this is due to the relative importance of language functions when the hemisphere is taxed beyond its available resources (Strauss et al., 1990). Essentially, the language functions crowd out other functions in Darwinian fashion because of their adaptive importance. This suggests that language functioning would be spared among patients with lesions in the left temporal lobe, but these patients would demonstrate impairment on nonverbal tasks.

Researchers who have found this pattern of sparing verbal functions at the expense of nonverbal functions have concluded that it provides support for the crowding hypothesis (Lidzba, Staudt, Wilke, Grodd, et al., 2006). Furthermore, some researchers have found a positive correlation between atypical hemispheric dominance for language and nonverbal deficits (Lidzba, Staudt, Wilke, Grodd, et al., 2006). Nevertheless, these findings are inconsistent in the literature, as rates of both verbal and nonverbal impairments and their co-occurrence vary across studies (Strauss et al., 1990), suggesting these constructs and factors influencing them are not well understood. Moreover, there are problems with the research supporting the crowding hypothesis, such as small sample size (Lidzba, Staudt, Wilke, Grodd, et al., 2006; Strauss et al., 1990). It appears that these findings are more consistent in individuals who sustain the injury to the left hemisphere prior to age 6 (Lidzba, Staudt, Wilke, Grodd, et al., 2006; Straus et al., 1990), but there have been exceptions here as well (Sveller et al, 2006). Although some research supports the crowding hypothesis, the results are inconsistent.

For patients with temporal lobe epilepsy, impairments demonstrated outside of that focal region should be explained to help doctors and patients make informed decisions about treatment. Possible explanations for patients with temporal lobe epilepsy who demonstrate nonverbal impairments include the crowding hypothesis or the possibility of more diffuse injury, such as an additional seizure focus. If the latter is the case, it may be necessary to find and monitor this location. Additionally, helping patients identify and plan for the risks of surgery, such as a decline in specific cognitive skills, can help them make informed decisions as to whether to have the surgery. Furthermore, if there is more diffuse injury, the surgery may not have the intended result and may alter the recommendations of the treatment team.

Purpose of the Study

The purpose of the study was to determine the prevalence of the crowding pattern and the prevalence of cognitive reserve in typically organized and atypically organized patients with temporal lobe epilepsy. A second purpose of this study was to determine whether neuropsychological test data predicts hemispheric dominance for language in patients with temporal lobe epilepsy. To assess these variables, retrospective data collected from the neuropsychological reports of Wada and functional magnetic resonance imaging (fMRI) data by a board certified neuropsychologist was used. Specifically, the Wada language data and fMRI verb generation data were used to confirm hemispheric dominance for language. The data were used to evaluate the prevalence of crowding in typically and atypically organized individuals and the prevalence of cognitive reserve in this sample. Finally, neuropsychological data was used to explore whether it can predict hemispheric dominance for language in patients with temporal lobe epilepsy. It was expected that there would be a difference in the prevalence of crowding and cognitive reserve in patients with temporal lobe epilepsy and typical or atypical hemispheric dominance for language. It was predicted that distinct neuropsychological profiles would be able to distinguish between hemispheric dominance for language groups.

Chapter 2: Literature Review

Hemispheric Dominance

Identifying the dominant hemisphere for language is crucial for patients considering neurosurgery because of the risk of cognitive impairments following surgery (Eliashiv et al., 2014). In patients with brain lesions, it is necessary to identify how brain organization may be altered due to the pathology of the lesion (Arora et al., 2009). This knowledge may alter the neurosurgeon's recommendations or the patient's decision to proceed with the surgery (Arora et al., 2009; Drane et al., 2012). There is always a risk of cognitive impairments following neurosurgery; however, the risk can be minimized by the surgeon's awareness of the patient's brain organization.

The left hemisphere has long been noted for its importance in language functioning (Donaldson & Johnson, 2006; Powell et al., 2012). Broca's and Wernicke's areas, historically considered to be the speech areas of the brain, are located in the left cerebral hemisphere and result in a left cerebral dominance for language in the majority of humans (Donaldson & Johnson, 2006; Sveller et al., 2006). Rates of left hemispheric dominance for language in right-handed individuals varies between 80% and 97% (Donaldson & Johnson, 2006; Mazoyer et al., 2014; Powell et al., 2012; Sveller et al., 2006). The majority of left-handed individuals also demonstrate left hemispheric dominance for language with rates falling between 74% and 78% (Powell et al., 2012). The reasons for a single hemisphere controlling language functioning are still being explored, but include cerebral economy and efficiency as well as to minimize confusion for the vocal chords and larynx (Donaldson & Johnson, 2006). Regardless of the reason for its development, hemispheric dominance for language is in the left cerebral hemisphere for the majority of individuals.

Language functions and the effective use of language are a complex concept that constitutes a neuronal network and involves areas in the frontal, temporal, and parietal regions (Price, 2000). The temporal lobe is involved in a number of language functions, including confrontation naming, comprehension, and higher order language functions (Price, 2000; Tracy & Boswell, 2007). The hippocampus, specifically, has also been found to be involved in language tasks, including comprehension (Bartha et al., 2005). Furthermore, patients with mesial temporal lobe epilepsy (MTLE) have demonstrated language impairments, with confrontation naming problems being the most frequent complaint (Tracy & Boswell, 2007). The results from studies involving both insult/injury and functional neuroimaging suggest that the temporal lobe plays an important role in language functioning.

Atypical hemispheric dominance. Atypical hemispheric dominance for language occurs when language is under control of the right hemisphere or both hemispheres (Drane et al., 2012; Lidzba, Staudt, Wilke, Grodd, et al., 2006; Mazoyer et al., 2014; Powell et al., 2012). The gold standard for assessing hemispheric dominance for language has been the intracarotid amobarbital procedure, also known as the Wada, since its application in 1955 (Moddel, Lineweaver, Schuele, Reinholz, & Loddenkemper, 2009); however, the procedure for the Wada test is invasive (Arora et al., 2009; Drane et al., 2012). Functional magnetic resonance imaging (fMRI) is an alternative procedure that has been used to assess hemispheric dominance for language (Drane et al., 2012). The advantages of fMRIs include the procedure being noninvasive and more easily replicated (Arora et al., 2009). These procedures show a high rate of concordance in identifying individuals with atypical hemispheric dominance for language (Arora et al., 2009). Due to the noninvasive nature of the fMRI, many hospitals are utilizing fMRIs to determine hemispheric dominance for language and reserving the Wada procedure for individuals whose fMRI results are equivocal (Arora et al., 2009). The Wada procedure and fMRIs are an effective means of identifying hemispheric dominance for language and can be used in conjunction with each other if one test is inconclusive.

Rates of atypical hemispheric dominance for language are low in the general population, with right or bilateral language representation estimated to be between 0.4% and 11% of right-handed individuals and up to 22% of left-handed individuals (Araujo et al., 2009; Drane et al., 2012; Lidzba, Staudt, Wilke, Grodd, et al., 2006; Powell et al., 2012; Spreer et al., 2001). The occurrence of atypical hemispheric dominance in epilepsy patients has been found to be higher than that of the general population, with 20% to 33% of patients demonstrating atypical hemispheric dominance (Araujo et al., 2009). More specifically, right hemispheric dominance rates have been found between 2% and 10% of epilepsy patients and bilateral language representation has been found between 5% and 25% of epilepsy patients (Drane et al., 2012). Higher rates of atypical hemispheric dominance have also been found in patients with left hemispheric lesions (Lidzba, Staudt, Wilke, Grodd, et al., 2006). Right hemispheric dominance for language was found in 19.7% of patients and bilateral language representation in 9.6% of Rasmussen and Milner's (1977) landmark study of patients with left hemisphere lesions. Rates of atypical hemispheric dominance are relatively rare in the general population, suggesting the higher rates of atypical hemispheric dominance of patients with brain lesions are related to the presence of the lesion.

Explaining atypical hemispheric dominance. The higher rates of atypical hemispheric dominance for language in patients with brain lesions are representative of the brain's plasticity and capacity for reorganization to spare language functioning (Lidzba, Staudt, Wilke, Grodd, et al., 2006). Four conceptual models, functional redundancy, functional substitution, cognitive control, and cognitive reserve, have been identified from functional neuroimaging studies as ways in which the brain can adapt to injury or disease (Tracy & Osipowicz, 2011). The distinguishing patterns result from whether the change is the result of a specific cognitive mechanism or general cognitive functions, as well as whether there is evidence of latent connectivity prior to the injury (Tracy & Osipowicz, 2011).

Functional redundancy is evident when there is a loss of a function that has duplicate representation elsewhere in the brain (Tracy & Osipowicz, 2011). This duplicate representation is then revealed after the injury and incorporated into the neuronal network (Tracy & Osipowicz, 2011). This is identified on functional neuroimaging when there is evidence of latent connectivity on pre-injury scans and involves a specific, as opposed to a general, cognitive mechanism (Tracy & Osipowicz, 2011). Functional substitution is when a new component is added into the network to compensate for the loss of a function (Tracy & Osipowicz, 2011). It involves a specific cognitive mechanism, but there is no evidence of latent connectivity on pre-injury scans (Tracy & Osipowicz, 2011). Cognitive control involves the use of monitoring and supervisory systems (Tracy & Osipowicz, 2011). It involves general cognitive mechanisms, with no evidence of latent connectivity on pre-injury scans (Tracy & Osipowicz, 2011). Finally, cognitive reserve is the availability of restorative and resilient functions above and beyond cognitive control (Tracy & Osipowicz, 2011). It involves general cognitive mechanisms, with evidence of latent connectivity on pre-injury scans (Tracy & Osipowicz, 2011). It is possible that any of the four conceptual models could explain the behavioral observation proposed by the crowding hypothesis. It is out of the scope of this study to test all four hypotheses, but the most researched of these is cognitive reserve theory.

Cognitive reserve theory. A comparable degree of brain pathology can result in varying clinical manifestations (Akman et al., 2003; Satz, Cole, Hardy, & Rassovsky, 2011; Stern, 2009). Efforts have been made to explain how similar pathology or injury can have different clinical presentations and courses of recovery (Stern, 2009). Two such attempts to explain the indirect effect of brain lesions on impairment are reserve and cognitive reserve (Satz et al., 2011). The concept of reserve proposes that individual differences in the brain, such as the size of the brain or the number of neurons and synapses, can explain the variability seen in individuals coping with brain pathology (Satz et al., 2011). Furthermore, individual differences in brain anatomy are due to life experiences and their effect on neurogenesis (Stern, 2009; Sumowski & Leavitt, 2013). Therefore, the concept of reserve is a static concept, in which there is a fixed threshold for impairment for each individual that varies based on the amount of reserve an individual has.

Conversely, cognitive reserve theory proposes that the individual variability seen in response to brain injury is due to individual differences in cognitive processing, or neuronal networks, on performance (Satz et al., 2011; Stern, 2009). The focus in cognitive reserve theory is on individual differences in processing, rather than solely on individual differences in anatomy. As such, cognitive reserve theory is an active model in which the brain attempts to adapt to damage by using preexisting networks or compensatory processes (Satz et al., 2011; Stern, 2009). Because cognitive reserve theory is an active model that focuses on neuronal networks, unlike reserve, it does not propose a fixed cutoff for impairment (Stern, 2009). As such, the focus of cognitive reserve theory is the process that allows patients with neuropathology to maintain functioning (Stern, 2009). Both reserve and cognitive reserve have been used to explain individual differences in the clinical presentation of brain pathology, but differ in that the brain takes a passive role in reserve theory but an active one in cognitive reserve theory.

The demarcation between reserve and cognitive reserve is not clear-cut because they influence each other and are due to similar factors (Satz et al., 2011;

Stern, 2009). Both reserve and cognitive reserve propose that individual differences in the clinical manifestation of the brain pathology are due to past experiences (Stern, 2009; Sumowski & Leavitt, 2013). Patients with higher reserve are less susceptible to cognitive impairment because patients with larger brains or more neurons and synapses can withstand a greater insult before seeing an impact on functioning (Sumowski & Leavitt, 2013). Cognitive reserve theory posits that cognitive functioning is preserved in some individuals because of the efficiency or plasticity in the brain networks (Sumowski & Leavitt, 2013). Factors that influence levels of cognitive reserve include premorbid intelligence, education, and occupation (Akman et al., 2003; Stern, 2009), and have been referred to as "an intellectually enriching lifestyle" in the literature (Sumowski & Leavitt, 2013, p. 1123. Furthermore, factors that promote neuronal plasticity are regulated by exercise and cognitive stimulation (Stern, 2009). Education, occupation, and intellectual stimulation are considered to be the factors that make up the enriched environment that contributes to an individual's cognitive reserve.

Underlying mechanism of cognitive reserve theory. The underlying neuronal mechanism explaining cognitive reserve theory is hippocampal neurogenesis (Pai & Tsai, 2005; Stern, 2009). Neurogenesis is the growth of new functional neurons from neural precursor cells (Ruan et al., 2014). Historically, neurogenesis was believed to cease in the early post-natal period (Ruan et al., 2014). This view was first challenged in the 1960s by Altman et al., who found that neurogenesis was possible in the hippocampus (Ruan et al., 2014). Since then, other studies have found that hippocampal neurogenesis is possible in adult humans, rodents, and primates (Ruan et al., 2014). Hippocampal neurogenesis is the growth of new neurons in the hippocampus, particularly the subventricular zone and subgranular zone, as well as the dentate gyrus (Kempermann et al., 2002; Ruan et al., 2014; Stern, 2009). Neural stem cells and neural progenitor cells from these areas produce new functional neurons and glia over the course of a mammal's lifetime (Ruan et al., 2014). Hippocampal neurogenesis explains reserve and cognitive reserve: it increases the number of neurons, as reserve would propose, but with the increase in neurons comes a shift in neuronal networks, as cognitive reserve would propose.

Neurogenesis is a process that consists of four stages: cell proliferation, migration, differentiation, and integration (Ruan et al., 2014). Lesions in the brain produce a cascade of events, including neuronal death and axonal injury (Ruan et al., 2014). The four stages of neurogenesis are contributory factors in adapting to and limiting impairments related to brain lesions (Ruan et al., 2014). Adult neurogenesis can occur as a result of any pathological change in the hippocampus (Ruan et al., 2014). The process of neurogenesis is triggered by the pathological change and results in adaptation to the pathological change. Neurogenesis plays a role in cognitive reserve in two ways, before the onset of the disease or injury and in response to the disease or injury. An enriched lifestyle results in neurogenesis and contributes to an increase in neuronal networks over the lifespan, but it also allows the brain to adapt to insult or injury by creating new or strengthening alternative networks from those injured.

Research supporting cognitive reserve theory. Cognitive reserve theory has been applied to various neuropathological disorders, including dementia, stroke, traumatic brain injury (TBI), multiple sclerosis (MS), and epilepsy (Akman et al., 2003; Nunnari, Bramanti, & Marino, 2014). The bulk of the research has been conducted in patients with dementia, where it was first recognized that individuals who have higher cognitive reserve perform better for longer periods of time than those with less cognitive reserve (Akman et al., 2003). Additionally, in patients with Alzheimer’s disease (AD), individuals with more cognitive reserve have been found to have greater AD pathology when they receive the diagnosis (Stern, 2009). Further, the risk of developing AD was greater for patients with fewer than 8 years of education, and even worse for those with less education and low occupational attainment (Stern, 2009). Ongoing intellectual and social stimulation have also been found to increase cognitive reserve and lower the risk of developing dementia (Stern, 2009). Nevertheless, once AD pathology emerges, patients with higher cognitive reserve demonstrate a more rapid decline and died sooner than those will less cognitive reserve (Stern, 2009). Although this may seem counterintuitive, because patients with higher cognitive reserve have greater AD pathology before showing symptoms, the disease has progressed further in these patients at the time of diagnosis (Stern, 2009). Therefore, patients with higher levels of cognitive reserve are not spared from the progression of the disease, but the duration, due to the delayed onset.

There is less research on cognitive reserve theory as it relates to other cognitive disorders (Nunnari et al., 2014). Stroke patients with higher education levels have been shown to have less cognitive decline than the patients with lower education levels (Nunnari et al., 2014). Cognitive reserve has also been applied to patients with TBI (Nunnari et al., 2014); however, because TBIs are most likely to occur early in life before an individual has completed his or her educational or occupational goals, cognitive reserve may be more limited in these individuals (Nunnari et al., 2014). Nevertheless, low IQ and low educational level have been correlated with an increase in cognitive impairments (Nunnari et al., 2014). Neurogenesis has been found to occur in stroke patients as well as patients with TBI, further suggesting cognitive reserve theory can be applied to these patients (Ruan et al., 2014). Cognitive reserve has also been applied to patients with MS, with those with higher intellectual attainment and larger maximum lifetime brain growth showing less cognitive impairments than those with lower intellectual attainment and less maximum lifetime brain growth (Sumowski & Leavitt, 2013). Although there is less research on cognitive reserve theory in other cognitive disorders, there is strong evidence suggesting it can be applied to a more diverse population than dementia patients.

Cognitive reserve theory has also been considered in patients with epilepsy, to understand the variability in the severity of cognitive impairments that cannot be explained by the epileptogenic region. Patients with epilepsy demonstrate changes in brain structure and connectivity (Dabbs et al., 2012; Lin, Mula, & Hermann, 2012). In addition, individuals with childhood-onset epilepsy demonstrate a slowing of white matter growth and connectivity compared to controls (Hermann et al., 2010). Structural abnormalities have been found in patients with TLE that extend beyond the hippocampus and include subcortical structures and extratemporal lobe regions (Dabbs et al., 2012). Individuals with childhood-onset epilepsy are particularly susceptible to age related decline in their elderly years (Hermann et al., 2010). Nevertheless, despite neuroanatomical changes to diverse brain regions, those with higher educational and occupational attainment demonstrate less cognitive decline (Hermann et al., 2010). Higher education and occupational attainment appear to serve as protective factors against cognitive impairment despite a lower white matter volume and structural brain changes.

Studying cognitive reserve in patients with epilepsy is challenging due to the interplay between IQ, education, and access to quality health care (Akman et al., 2003). It is also confounded by factors such as type of epilepsy, age of epilepsy onset, and antiepileptic drug (AED) use (Pai & Tsai, 2005). Nonetheless, there is some promising research suggesting cognitive reserve theory is applicable to patients with epilepsy. In one such study, the researchers looked at the effect of education on cognitive impairment in epilepsy patients with a later age of seizure onset, after the patient had reached his or her highest level of education (Pai & Tsai, 2005). The researchers found that patients with higher educational attainment demonstrated better cognitive functioning (Pai & Tsai, 2005). Individuals with a later age of seizure onset and higher educational attainment had less cognitive impairments as a result of their epilepsy.

Problems with the research supporting cognitive reserve theory. Although there is a considerable body of research supporting cognitive reserve theory, there are problems with the research, including problems with the operational definition and fully understanding the underlying mechanism (Nunnari et al., 2014; Ruan et al., 2014; Satz et al., 2011). Cognitive reserve is a hypothetical construct that is measured indirectly by factors believed to influence cognitive reserve, such as education level (Nunnari et al., 2014); however, other factors that have the potential to influence cognitive reserve, such as leisure or social activities, are often ignored (Nunnari et al., 2014). Furthermore, little is known about how neurogenesis works. Specifically, how the cells migrate and integrate into new or existing neuronal networks and under what pathological conditions remain unclear (Ruan et al., 2014). Although there is compelling research for cognitive reserve theory, it is not without its problems and there are still many questions left unanswered.

Neuropsychological profiles in patients with temporal lobe lesions. Most of the research on neuropsychological profiles in patients with temporal lobe injury or insult has been in patients with temporal lobe epilepsy. Neuropsychological test results in patients with unilateral TLE vary depending on the hemisphere affected. Traditionally, patients affected by TLE in their dominant hemisphere demonstrate verbal memory and language deficits, whereas patients affected by TLE in their non-dominant hemisphere demonstrate visual memory deficits (Gargo et al., 2013). Extratemporal lobe deficits are likely for some patients with TLE, given the structural abnormalities demonstrated in neuroimaging studies (Gargo et al., 2013). These deficits may be contralateral to the side of seizure onset or those typically associated with frontal or parietal lobe deficits. Research has suggested that as many as 75% of patients with MTLE with hippocampal sclerosis (HS) had atypical memory profiles (Gargo et al., 2013). Four atypical memory profiles have been identified: memory deficits in the contralateral temporal lobe to the epileptogenic region, bitemporal memory deficits, a normal memory profile, or a general cognitive impairment profile (Gargo et al., 2013). No difference between the groups was found regarding gender, age at seizure onset, age at evaluation, or epilepsy duration (Gargo et al., 2013). Another study found that the majority of their sample was impaired on more than one cognitive domain, which was suggestive of generalized impairments (Wang et al., 2011). A traditional neuropsychological profile has been determined for patients with unilateral TLE, but neuroimaging studies and neuropsychological testing suggest that TLE patients experience deficits in regions outside of their epileptic region. Furthermore, there is limited discussion of other cognitive domains, such as attention and executive functions, that influence memory in patients with TLE. The patient profile and potential risk factors are still unclear.

The crowding hypothesis. The crowding hypothesis is a behavioral observation that has been used to describe the relative sparing of language functioning in the presence of left hemisphere lesions (Satz, Strauss, Hunter, & Wada, 1994; Strauss et al., 1990). The first attempts to explain the sparing of language functioning in the presence of an early lesion observed that these individuals also demonstrated deficits in nonverbal functions (Lansdell, 1969; Satz et al., 1994). The crowding hypothesis was proposed by Teuber in 1974 and suggests that this phenomenon is due to the relative importance of language functions and the competition for space in a taxed right hemisphere (Strauss et al., 1990). Because of its adaptive importance, language functions “crowd out” other, nonverbal functions.

Research supporting the crowding hypothesis. The crowding hypothesis has been demonstrated in the literature with both epileptic and non-epileptic populations (Lidzba, Staudt, Wilke, & Kageloh-Mann, 2006). A consistent finding has been nonverbal impairments in patients whose language functions have been reorganized to the right hemisphere (Lidzba, Staudt, Wilke, & Kageloh-Mann, 2006; Strauss et al., 1990; Teuber, 1974). Further, some studies have shown that patients with atypical hemispheric dominance for language have limited impairments on verbal tasks (Strauss et al., 1990). Although verbal functioning was affected, the primary impairments were on nonverbal functions that are typically associated with the non-dominant hemisphere (Strauss et al., 1990). Additionally, the degree of right hemispheric dominance for language influenced performance on nonverbal tasks (Lidzba, Staudt, Wilke, & Kageloh-Mann, 2006). The greater the degree of reorganization to the right hemisphere, the greater the impairments were on nonverbal tasks (Lidzba, Staudt, Wilke, & Kageloh-Mann, 2006). This suggests that when language is reorganized, impairments can be seen in nonverbal functions as a result of verbal functions competing for space.

Problems with the research supporting the crowding hypothesis. Research supporting the crowding hypothesis has been criticized for problems related to methodology (Satz et al., 1994). First, there are concerns regarding the tasks used to assess functioning and the focus on verbal and performance IQ while neglecting nonverbal tasks (Satz et al., 1994). Second, many of the studies supporting the crowding hypothesis have failed to assess for hemispheric dominance (Satz et al., 1994). Finally, many of the studies have relatively small sample sizes (Satz et al., 1994; Strauss et al., 1990). Due to these methodological flaws, questions regarding the validity and generalizability of these studies have been raised (Satz et al., 1994). It is necessary to address these methodological flaws to increase the strength and generalizability of the crowding hypothesis as an explanation for patients with atypical hemispheric dominance for language and nonverbal deficits.

Relatively recently, the crowding hypothesis has been criticized for being too simplistic (Lidzba, Staudt, Wilke, Grodd, et al., 2006). This is particularly difficult to reconcile with the modern view of the human brain as being an arrangement of cortical networks that is flexible in nature (Lidzba, Staudt, Wilke, Grodd, et al., 2006). As such, to truly understand the reorganization of verbal and nonverbal functions, longitudinal studies assessing functioning over time are needed (Lidzba, Staudt, Wilke, Grodd, et al., 2006). For example, one longitudinal study found early age of seizure onset in epilepsy patients was related to a worse overall trajectory (van Iterson, Zijlstra, Augustijn, van der Leij, & de Jong, 2014). Although there appeared to be an initial sparing of verbal functioning, there was a more pronounced decline thereafter (van Iterson et al., 2014). These results suggest that verbal functions may have been initially spared but will eventually decline (van Iterson et al., 2014). Understanding how and when the connections are made, and assessing other factors potentially influencing this variable can help explain how brain plasticity changes over the course of development.

One study found that atypical hemispheric dominance for language and an early age of seizure onset were associated with both verbal and nonverbal functional impairments; however, atypical hemispheric dominance for language coupled with a later age of seizure onset was associated with verbal impairments, whereas nonverbal functions were relatively unaffected (Satz et al., 1994). This suggests that a modification to the crowding hypothesis may be in order. Although individuals with atypical hemispheric dominance still demonstrated language impairments (Satz et al., 1994), the impairments may be to a lesser extent than would be expected if language functioning remained in the right hemisphere (Strauss et al., 1990). This effect can be explained by the developmental processes of myelination and dendritic pruning, as these are the means by which the brain fine tunes neuronal systems during development (Casey, Tottenham, Liston, & Durston, 2005). This effect may also be influenced by ongoing seizures in patients with atypical hemispheric dominance, as their seizure disorders were long-standing (Satz et al., 1994). The ability of the brain to adapt and reorganize following seizure onset may be impacted by seizure frequency.

Age of seizure onset. Age of onset is an important variable to consider when discussing the preservation of language functioning because of the impact of age on brain plasticity (Lidzba & Staudt, 2008). Insult or injury acquired while in utero or during infancy can be more easily compensated for than those acquired later in life (Lidzba & Staudt, 2008). Age of seizure onset has been demonstrated in the literature as impacting reorganization and deficit pattern in patients with LTLE (Satz et al., 1994). Furthermore, a greater percentage of individuals with atypical hemispheric dominance for language sustained the lesion prior to age 6 (Strauss et al., 1990). The crowding hypothesis has been found more consistently in patients who sustain the lesion prior to age 6 (Lidzba, Staudt, Wilke, Grodd, et al., 2006; Strauss et al., 1990). This has been a consistent finding in most of the current research, but there have been a few exceptions (Sveller et al, 2006).

Differences in brain structure and connectivity have also been found between children with epilepsy and typically developing children (Dabbs et al., 2012; Hermann et al., 2010). Cerebral gray matter changes are comparable for patients with childhood or adolescence seizure onset and controls, but significant differences were found on white matter changes between the groups (Hermann et al., 2010). The control group demonstrated an increase in white matter volume, whereas there was no change in white matter volume in patients with childhood-onset epilepsy (Hermann et al., 2010). Age of onset impacts typical neurodevelopment and the brain’s ability to adapt to the lesion, and the extent to which the brain is able to reorganize to compensate for the lesion.

Summary

Atypical hemispheric dominance is rare in the general population (Araujo et al., 2009; Drane et al., 2012; Lidzba, Staudt, Wilke, Grodd, et al., 2006; Powell et al., 2012; Spreer et al., 2001). The higher rates of atypical hemispheric dominance in the presence of a left hemispheric lesion suggest that the rates are due to the brain's attempt to adapt to the pathology. Many models have been laid forth to explain the brain's ability to adapt to disease. Cognitive reserve is the most researched of the models, and has been shown to be an important factor influencing deficit in the face of injury. The crowding hypothesis is a behavioral observation that could be the result of any of the four models or some combination of the models. The prevalence of crowding and cognitive reserve in patients with TLE with typical and atypical hemispheric dominance for language is unknown. This study explored the prevalence of crowding and cognitive reserve in patients with temporal lobe epilepsy. Additionally, the study aimed to determine whether neuropsychological patterns in patients with temporal lobe epilepsy are predictive of hemispheric dominance for language.

Chapter 3: Hypotheses

The main goal of the current study was to determine the prevalence of the crowding pattern and the prevalence of cognitive reserve in typically and atypically organized patients with temporal lobe epilepsy. A second goal of this study was to explore whether neuropsychological test data can predict hemispheric dominance for language.

- The first hypothesis proposed that the prevalence of patients with TLE who demonstrate the crowding pattern on neuropsychological test data would be higher in the atypical hemispheric dominance group than patients from the typical hemispheric dominance group.
- The second hypothesis proposed that the prevalence of cognitive reserve in patients with TLE in the atypical hemispheric dominance group would differ from patients from the typical hemispheric dominance group.
- The third hypothesis proposed that neuropsychological testing can predict hemispheric dominance for language. Language, in addition to attention, executive functioning, visuospatial functions, verbal memory, visuospatial memory, and sensory motor functions, are domains assessed in a neuropsychological test battery. Patients with atypical hemispheric dominance for language were hypothesized to demonstrate a different deficit pattern on neuropsychological testing than patients who are typically organized. Regarding the rationale for this hypothesis, although it has traditionally been believed that patients affected by TLE in their dominant hemisphere will demonstrate verbal memory and language deficits and patients affected by TLE in their non-dominant

hemisphere demonstrate visual memory deficits, as much as 75% of patients with MTLE with HS had atypical memory profiles (Gargo et al., 2013). This also does not take into account other cognitive domains that may influence memory such as attention or executive functions.

Chapter 4: Methodology

This study retrospectively reviewed charts of patients who presented to an urban hospital in southeastern Pennsylvania as potential pre-surgical candidates for neurosurgery between 1995 and 2015.

Participants

Participants were selected from patient archives from the hospital. Patients were potential pre-surgical candidates for neurosurgery who underwent Wada and/or fMRI testing to determine hemispheric dominance for language and neuropsychological testing as part of the comprehensive evaluation.

Participants were assigned to the typical hemispheric dominance group, left hemisphere (control group), or the atypical hemispheric dominance group, right or bilateral hemispheres based on a board certified clinical neuropsychologist's interpretation of Wada and fMRI data.

Inclusion criteria. In addition to having undergone a laterality test to determine hemispheric dominance, other inclusion criteria include having completed the verb generation task for patients who were evaluated with an fMRI, having a unilateral TLE, and having undergone a formal neuropsychological evaluation.

Exclusion criteria. Exclusion criteria include patients who have lesions in addition to unilateral TLEs (e.g. bilateral or extratemporal), patients whose laterality testing is inconclusive (i.e., both hemispheres are needed to support language functioning), patients evaluated post-surgery, patients with an IQ less than 70, and patients whose cognitive expenditure is questionable (TOMM Trial 2 < 45).

Setting and Apparatus

Setting. The setting for the study was department of neurology at an urban university hospital in southeastern Pennsylvania.

Apparatus. Language lateralization was determined by a board certified neuropsychologist's interpretation of Wada and/or fMRI data.

Wada. The Wada test has been the gold standard for determining hemispheric dominance for language in neurosurgery candidates since its inception (Drane et al., 2012). The Wada test involves the injection of a barbiturate in the intracarotid, which results in the transient paralysis of one of the hemispheres (Strauss et al., 1990). With the hemisphere paralyzed, it is possible to test language functioning and determine hemispheric dominance (Strauss et al., 1990). If the patient is unable to communicate when that hemisphere is paralyzed, language is under control of that hemisphere.

fMRI. FMRI has been used increasingly to determine hemispheric dominance for language, due to the invasive nature of the Wada test. Many patients were assessed for hemispheric dominance for language by fMRIs instead of or in addition to the Wada test. For these patients, the laterality index and a verb generation task was used to determine hemispheric dominance for language by a board certified neuropsychologist.

Concordance between Wada and fMRI. The Wada test and fMRIs were used to determine hemispheric dominance for language with an increasing number of hospitals transitioning from the Wada to fMRIs. The Wada test has been falling out of favor due to the invasive nature, discomfort for the patients, and the inability to localize functions (Arora et al., 2009). Furthermore, there is a high concordance between the two tests (91.3%) in the ability to identify hemispheric dominance for language (Arora et al., 2009). Because of this high concordance, patients who were given either or both of these tests were included in the study.

Independent variables. Scores from patients' neuropsychological tests prior to surgery were used as measures of cognitive functioning in the following domains: attention, executive functions, language, visuospatial skills, verbal memory, visuospatial memory, and sensory motor skills.

Attention. Digit Span (DS) from the Wechsler Adult Intelligence Scale, third edition (WAIS-III; Wechsler, 1997a) and the Wechsler Adult Intelligence Scale, fourth edition (WAIS-IV; Wechsler, 2008) was used to assess attention.

*Digit Span***.** DS is a measure of attention that requires the subject to repeat a string of numbers. The DS subtest of the WAIS-III (Wecshler, 1997) is a composite of two scores: Digit Span Forward (DSF), during which the subject is required to repeat a string of numbers in order, and Digit Span Backward (DSB), which requires the subject to repeat a string of numbers backward. Reliability coefficients for DS from the WAIS-III are above .90 (Strauss, Sherman, & Spreen, 2006). The WAIS-IV (Wechsler, 2008) also includes DSF and DSB, in addition to Digit Span Sequence (DSS). In DSS, the subject is required to repeat the string of numbers from lowest to highest. The WAIS-IV's DS has been found to be a valid and reliable measure of attention (r = .93; Wechsler, 2008), and DS from the WAIS-III correlates with DS from the WAIS-IV (r = .75; Wechsler, 2008).

Executive functions. The Wisconsin Card Sorting Test (WCST; Grant & Berg, 1981) and Trail Making Test B (TMT; Heaton, Miller, Taylor, & Grant, 2004) were used to assess executive functions.

Wisconsin Card Sorting Test. The WCST is a measure of executive functioning that assesses abstract reasoning and set shifting ability when faced with changing stimuli. The task consists of four stimulus cards that depict four forms, four colors, and four numbers. The subject is required to sort the response card based on a variable unknown to the subject. During the test, the unknown variable switches, requiring the subject to respond to feedback and adapt. The total number of errors scale from the WCST is a reliable and valid measure of executive functioning with a test-retest reliability coefficient of .66 (Strauss et al., 2006). Some have argued that the WCST should not be used to reassess problem solving skills for individuals with intact memory. Once the individual determines the categories and shift principle, these individuals are able to complete the task rapidly and successfully (CITATION).

Trail Making Test B. The TMT is a measure of executive functioning that requires the subject to rapidly scan and sequence letters and numbers in order by connecting the appropriate dot. The subject is required to draw a straight line from each dot, alternating between a number and a letter in order. Test-retest reliability has been shown to vary based on age, education, and clinical conditions, and range from .44 to .89 (Strauss et al., 2006).

Language. The total score on the Controlled Oral Word Association Test (COWAT), the total score on Animal Naming, and the total score on the Boston Naming Test (BNT) were used to assess verbal ability (Heaton et al., 2004). Correlations between phonemic and semantic fluency tasks have been found to be moderate (r = .34-.64). Correlations are higher between BNT and semantic fluency (r = .57–.68) than between the BNT and phonemic fluency (r = .43–.50; Strauss et al., 2006).

Controlled Oral Word Association Test. The first measure that was used to assess language functions is the COWAT. In this task, the subject must generate as many words as possible from a target letter within 1 minute. The total score is based off of the combined score from three trials, with the target letter changing with each trial (F A S). The COWAT is a valid and reliable measure of phonemic fluency with test-retest reliability above .70 (Strauss et al., 2006).

Animal Naming. The second measure that was used to assess language functions is the Animal Naming Test. In this task, the subject is to list as many different types of animals as possible within 1 minute. Animal naming is a valid and reliable measure of phonemic fluency, but the test-retest reliability range is large, falling between .47 and .79 (Strauss et al., 2006).

Boston Naming Test. The third measure that was used to assess language functions is the BNT. In this task, the subject is to name 60 different line drawings. The total score based on the Heaton norms are considered to be a reliable and valid measure of confrontation naming (Strauss et al., 2006). Test-retest reliability is ranges between .62 and .94 (Strauss et al., 2006).

Visuospatial skills. Block Design from the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) and the WAIS-IV (Wechsler, 2008) was used to assess visuospatial skills.

Block Design. Block design was used to assess visuospatial skills. In this task, the subject is required to manipulate blocks to make the tops of their blocks match an image provided. Block design is a valid and reliable measure of visuospatial skills (Wechsler, 2008). The reliability coefficient for block design from the WAIS-IV is .87 (Wechsler, 2008). The reliability coefficient for block design from the WASI is above .92 (Strauss et al., 2006).

Verbal memory. To assess verbal short-term memory, the California Verbal Learning Test, First or Second Edition (CVLT; Delis, Kramer, Kaplan, & Ober, 1987; CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000) and the logical memory subtest from the Wechsler Memory Scale, Third or Fourth Edition (WMS-III; Wechsler, 1997b; WMS-IV; Wechsler, 2009) were used.

California Verbal Learning Test. The CVLT and CVLT-II were used to assess verbal memory. The CVLT and CVLT-II are considered to be reliable and valid measures of verbal memory (Strauss et al., 2006). Three scores from the CVLT-II were analyzed: Total Learning on Trials 1-5, Immediate Free Recall, and Delayed Free Recall. The three scales have test-retest reliability coefficients of .80 or higher (Delis et al., 2000). The CVLT and CVLT-II correlate well with one another (Total Learning on Trials 1-5, $r = .76$; Strauss et al., 2006).

Wechsler Memory Scale – Logical Memory. The WMS-III and WMS-IV Logical Memory subtests are considered to be reliable and valid measures of verbal memory (Wechsler, 1997b; Wechsler, 2009). In this task, the subject is asked to recall two short stories immediately following the reading and after a 30-minute distraction filled delay. Two scores were analyzed: Immediate Recall and Delayed Recall. Reliability coefficients for immediate recall range between .82 and .86, and reliability coefficients for delayed recall range between .85 and .97 (Wechsler, 2009).

Visuospatial memory. To assess visuospatial short-term memory, the Designs subtest from the WMS-IV (Wechsler, 2009), the Visual Reproduction and Facial Memory from the WMS-III (Wechsler, 1997b) subtests were used. Because of the variability in the visuospatial memory tests administered over the period data were collected, visuospatial memory composites were developed from the Visual Reproduction and Design Memory tests. Scores were converted to T scores, and a composite was developed for Visual Reproduction and Design Memory Immediate Recall and for Delayed Recall.

Wechsler Memory Scale - Visual Reproduction. The WMS-III Visual Reproduction subtest is considered to be reliable and valid measures of visuospatial memory (Wechsler, 1997b). Two scores were analyzed: Immediate Recall and Delayed Recall. The reliability coefficients for immediate and delayed recall from the WMS-III were high, falling above.80 (Strauss et al., 2006).

Wechsler Memory Scale – Design Memory. The WMS-IV Design subtest is considered to be reliable and valid measures of visuospatial memory (Wechsler, 2009). Two scores were analyzed: Immediate Recall and Delayed Recall. The Design subtest is a valid and reliable measure of visuospatial memory (.85 for both immediate and delayed recall; Wechsler, 2009).

Wechsler Memory Scale – Facial Memory. The WMS-III Facial Memory subtest is considered to be reliable and valid measures of visuospatial memory (Wechsler, 1997b). Two scores were analyzed: Immediate Recall and Delayed Recall. The Faces subtest is a valid and reliable measure of visuospatial memory with adequate internal consistency (between .70 and .79 for both immediate and delayed recall; Strauss et al., 2006).

Sensory motor skills. To assess sensory motor skills, the Grooved Pegboard was used (Heaton et al., 2004).

Grooved Pegboard. The grooved pegboard task requires subjects to place pegs in a board as quickly as possible by using only one hand at a time. It is a reliable measure of fine motor skills, with marginal to high reliability coefficients (.67 to .86; Strauss et al., 2006).

Crowding. The crowding pattern has traditionally been operationalized as having spared verbal functions and impaired visuospatial functions. To test hypothesis 1, crowding was measured in two ways: as a binary and as a continuous variable. To test crowding as a binary variable, subjects were determined to have crowding if they had intact language ($T \geq 40$) on the average of the three language skills measures (COWAT, Animal Naming, and BNT) and impaired visuospatial functions ($T < 40$) on the visuospatial skill measure (Block Design). Subjects were determined to not have crowding if they had impaired language ($T < 40$) on the average of the three language skills measures (COWAT, Animal Naming, and BNT) and intact visuospatial functions ($T \geq 40$) on the visuospatial skill measure (Block Design). In this study, a continuous variable was developed to quantify the amount of crowding a subject demonstrates on language and visuospatial skills. To create this variable, the subject's normative scores on the language skills tasks (COWAT, Animal Naming, BNT) and the subject's normative scores on the visuospatial skills tasks (Block Design) were converted to T-scores. The mean of the language skills tasks was calculated. An index score was then developed: (mean of language skills tasks – visuospatial skills task)/(mean of language skills tasks + visuospatial skills task).

Cognitive reserve. Participants were grouped into having high or low levels of cognitive reserve, with those who score one standard deviation or higher on a premorbid IQ estimate as having high levels and those with one standard deviation or less as having low levels of cognitive reserve. Premorbid IQ was determined by the Wide Range Achievement Test reading subtest (WRAT-3 or WRAT-4; CITATION) and North American Adult Reading Test (NAART; Lezak, Howieson, Bigler, & Tranel, 2012). The WRAT is a measure of letter and word recognition (Strauss et al., 2006). The NAART is a test of word recognition (Lezak et al., 2012). Reading ability is used frequently as a proxy for premorbid IQ or premorbid functioning because reading ability is one of the most durable skills in the face of illness or injury (Lezak et al., 2012). The WRAT and the NAART have been found to be useful premorbid estimates of verbal IQ, but may underestimate performance or full scale IQ (Lezak et al., 2012). Reliability on the reading subtest from the WRAT-3 demonstrates is high (r = .90 or higher; Strauss et al., 2006). The NAART is among the most reliable neuropsychological tests, with high test-retest reliability (r = .92; Strauss et al., 2006). Performance on word reading tests is also related strongly to education level (Lezak et al., 2012). It is possible that this may reflect exposure or a more enriched lifestyle.

Dependent variables. Hemispheric dominance for language will be determined by a neuropsychologist's interpretation of WADA and/or fMRI data.

Procedure

This study was reviewed by the PCOM's Institutional Review Board. This study used archival data from an urban university hospital in southeastern Pennsylvania, which were collected during the comprehensive presurgical evaluation conducted on potential neurosurgery candidates. A board certified neuropsychologist determined hemispheric dominance for language from the Wada and/or fMRI data. Patients who underwent the Wada and fMRI procedures were consented prior to participating. Patients who underwent the Wada procedure were given an injection in the middle cerebral artery of sodium amytal through a catheter placed transfemorally (Tracy et al., 2009). Each hemisphere was injected independently, with a minimum of 45 minutes between injections (Tracy et al., 2009). Muscle strength and flaccidity were used to confirm hemiparesis (Tracy et al., 2009).

The procedure for patients who underwent fMRI testing to determine hemispheric dominance for language was described by Doucet et al. (2015): "All participants underwent Magnetic Resonance Imaging on a 3-T X-series Philips

Achieva clinical MRI scanner (Amsterdam, The Netherlands) using an 8-channel head coil. A total of 5 minutes of a resting-state condition was collected as well as a verb generation task to provide a measure of language hemispheric lateralization" (p. 290). The researcher was granted written permission and access to the SPSS data set from the hospital to use for this dissertation. The researcher reviewed the data set to ensure participants met the inclusion/exclusion criteria. All identifying information was removed, with each participant being assigned a random number for confidentiality prior to the researcher's acquisition of the dataset. The data were stored on the secure network at the hospital and on a flash drive kept in a locked on-site office. Statistics were run in SPSS.

Statistical Analyses

To test the three hypotheses, six statistical analyses were completed on the whole sample and three statistical analyses were completed on the RTLE sample and three on the LTLE sample. Because multiple statistical analyses were conducted on the same set of data, to reduce the risk of reporting significant findings by chance, the alpha level was adjusted with the Bonferroni correction. The sum of the alpha levels from the nine statistical analyses should be less than or equal to the overall alpha set at $\alpha = .05$. Therefore, each test will have an alpha level set at $\alpha = .005$.

An a priori power analysis was conducted to determine whether the sample size was large enough for statistical finding to be interpreted with confidence. With a sample size of 185, a medium effect size of .03, and an alpha set at .005, there was sufficient power to detect a difference for the chi-square analyses ($1-\beta = .78$); however, for the discriminant function analysis, with a sample size of 185, a medium effect size of .03, and an alpha set at .005, power was stringent ($1-\beta = .99$) and, as such, the results are interpreted with caution.

A post hoc power analysis was conducted for the logistic regression to determine whether the sample size was large enough to interpret statistical findings with confidence. With a sample size of 185 and an alpha set at .005, power was lenient ($1-\beta = .20$), leaving little ability to detect a difference if one exists and, as such, the results are interpreted with caution.

The goal of the current study was to determine the prevalence of the crowding hypothesis pattern (yes/no) and cognitive reserve (high/low) in patients with temporal lobe lesions (typical/atypical hemispheric dominance for language). To test the first and second hypotheses, a chi-square test for independence, an independent *t*-test, and a logistic regression were used. Chi-square can be used to determine whether there is a relationship between two nominal variables (Gravetter & Wallnau, 2013; McHugh, 2013). In a chi-square test for independence, a two-dimensional frequency distribution matrix is created by classifying each individual in the sample on both of the two variables (Gravetter & Wallnau, 2013). Therefore, a chi-square can be used to test whether the amount of crowding or cognitive reserve in patients who are typically organized for hemispheric dominance for language is significantly different from the amount of crowding or cognitive reserve in patients who are atypically organized for hemispheric dominance for language.

The first step in conducting a chi-square test for independence is to review all of the assumptions and restrictions that could cast doubt on the results (Gravetter & Wallnau, 2013). Chi-square tests assume independent observations, or subjects may be represented in only one cell (Gravetter & Wallnau, 2013). A second assumption of the chi-square test is that the size of the expected frequency of each cell is greater than 5 (Gravetter & Wallnau, 2013). The first assumption has been met because of the nature of the data. To ensure the second assumption is met, the expected values for each cell were calculated. The expected values should predict the number of patients in each category and the unbiased distribution if there is no effect from the crowding hypothesis pattern or cognitive reserve (McHugh, 2013). Once this was clarified, the observed values were compared to the expected values to determine whether the observed value is greater than what would be expected by chance (McHugh, 2013).

The first chi-square test was conducted to test whether there is a difference in incidence of the crowding pattern (yes/no) between patients with typical and atypical hemispheric dominance for language.

The second chi-square test was conducted to test whether there is a difference in incidence of cognitive reserve (high/low) between patients with typical and atypical hemispheric dominance for language.

An independent *t*-test is used when there are two experimental groups whose membership is exclusive to one of the two groups (Field, 2009). Assumptions that must be met prior to using a *t*-test include data are normally distributed and measured on at least an interval level, have roughly equal variances, and scores are independent (Field, 2009).

A logistic regression is used when there is one categorical dependent variable and there are multiple categorical and continuous independent variables (Field, 2009). In addition to understanding whether the atypical and typical hemispheric dominance groups differ on whether the subjects have crowding or cognitive reserve, a logistic regression tests whether the groups differ on the amount of crowding or reserve, as well as whether the groups differ from the interaction of crowding and cognitive reserve (Field, 2009). Assumptions that must be met prior to using a logistic regression include linearity, independence of errors, and multicollinearity. To test the assumption of linearity, the interaction between the predictor and its log transformation are used and deemed to have met the assumption if the interaction is not significant (Field, 2009). To test for the assumption of independence of errors, the Durbin-Watson test was used (Field, 2009). To test for the assumption of multicollinearity, tolerance and VIF statistics, eigenvalues of the scaled, uncentered cross-products matrix, the condition indexes and the variance proportions were computed (Field, 2009).

To test the third hypothesis, a discriminant function analysis was utilized to determine whether neuropsychological testing can predict hemispheric dominance for language. A discriminant function analysis is a methodology for group classification when there is one dependent variable with multiple predictor variables (Sheskin, 2007). This analysis can be used with predictor variables that are continuous and a dependent variable that is categorical when the groups are known prior to analysis (Sheskin, 2007). It is concerned with how well the combination of predictor variables can differentiate between the groups and predict group membership for a given subject (Sheskin, 2007). All predictor variables were converted to T scores. Subjects missing greater than 25% of the predictor variables were excluded. For the remaining subjects missing predictor variables, an average of the subjects' other predictor variables were calculated and used as a proxy for missing variables.

Assumptions that could be problematic for interpretation of the results if not met include multivariate normality, homogeneity of the variance-covariance matrices, linear relationships between all predictor variables within each group, and the absence of multicollinearity and outliers on the independent variables (Field, 2009; Sheskin, 2007). To test for multivariate normality, the univariate normality was checked for each dependent variable (Field, 2009). To test for homogeneity of the variance-covariance matrices, a Levene's test was used to test for univariate equality of variances between groups (Field, 2009). A Box's test was then employed to test for variance-covariance matrices. The assumption of random sampling assumes the data is measured at an interval level and randomly sampled (Field, 2009). The assumption of independence assumes that each observation is statistically independent (Field, 2009).

Chapter 5: Results

There were a total of 185 subjects who met the inclusionary and exclusionary criteria. Demographics of study participants are shown in Table 1.

Hypothesis I

A chi-square and a *t*-test were used to assess the first hypothesis. Of the 159 subjects who were typically organized, 149 (80.5% of the total sample) did not demonstrate the crowding pattern and 10 (5.4% of the total sample) demonstrated crowding. Of the 26 atypically organized subjects, 24 (13% of the total sample) of the subjects did not demonstrate crowding and 2 (1.1% of the total sample) demonstrated crowding. Of the 115 LTLE subjects, 95 were typically organized and 20 were atypically organized. Of the 95 LTLE subjects who were typically organized, 85 (73.9%) did not demonstrate crowding and 10 (8.7%) demonstrated crowding. Of the 20 LTLE atypically organized subjects, 18 (15.7%) did not demonstrate crowding and 2 (1.7%) demonstrated crowding. Of the 70 RTLE subjects, 64 (91.4%) were typically organized and 6 (8.6%) were atypically organized. None of the RTLE subjects demonstrated crowding. Due to the small sample size, Fisher's Exact test was used. The result of the chi-square analysis was insignificant, $X^2 = .678$. Results are displayed in Table 2. In addition, results of the *t*-tests were insignificant for the whole sample $t(177) = .84$, $p > .005$, the LTLE patients $t(109) = .28$, $p > .005$, and the RTLE patients $t(66) = .06$, $p > .005$. Results are displayed in Table 3.

Table 1

Clinical Information and Characteristics of Patients

	LTLE	RTLE
N (female)	58 (57)	38 (32)
Age (m ± std, years)	38.76 (1.46)	41.36 (1.98)
N Right-Handers (*N* Left-Handers)	86 (22)(1)	50 (11) (4)
Age of Seizure Onset (m ± std, years)	18.45 (1.78)	21.64 (1.91)
Full Scale IQ	97.41 (1.40)	100.34 (1.57)
Education (m ± std, years)	14 (0.30)	14 (0.37)
Hemispheric Dominance (right)	95 (20)	64 (6)
Crowding (Yes)	103 (12)	70 (0)
Cognitive Reserve (Yes)	79 (11)	50 (5)
Wada (atypical)	46 (10)	24 (3)
fMRI (atypical)	45 (8)	38 (2)
Wada and fMRI (atypical)	4 (2)	2 (1)
N Typical (female)	46 (49)	35 (29)
N Atypical (female)	12 (8)	3 (3)
N Right-Handed (atypical)	76 (10)	48 (2)
N Left-Handed (atypical)	13 (9)	7 (4)
N Ambidextrous (atypical)	0 (1)	4 (0)
Age of Onset Typical (m ± std, years)	18.58 (15.35)	20.99 (12.25)
Age of Onset Atypical (m ± std, years)	19.24 (6.49)	21.47 (10.34)
Education Typical (m ± std, years)	14.19 (2.53)	14.27 (2.32)
Education Atypical (m ± std, years)	13.9 (2.41)	14.67 (1.74)
Age of Typical (m ± std, years)	37.74 (12.29)	39.45 (12.96)
Age of Atypical (m ± std, years)	40.15 (11.22)	44.33 (12.89)

Note. Crowding and Cognitive Reserve scores documented are based off of binary estimates. RTLE = right temporal lobe epilepsy. LTLE = left temporal lobe epilepsy.

Table 2

Chi-Square Outcome for Hemispheric Dominance and Crowding

		No Crowding	Crowding	Total
RTLE				
	Typical	64	0	64
	Atypical	6	0	6
	Total	70	0	70
LTLE				
	Typical	85	10	95
	Atypical	18	2	20
	Total	103	12	115
Total				
	Typical	149	10	159
	Atypical	24	2	26
	Total	173	12	185

Note. Crowding was not calculated in RTLE patients because this would be the expected pattern and therefore not representative of crowding. RTLE = right temporal lobe epilepsy. LTLE = left temporal lobe epilepsy.

Table 3

T-test Outcome for Hemispheric Dominance and Crowding

	t	df	*p*	*Effect Size*
Whole Sample	.76	177	.84	.06
LTLE	.18	109	.28	.02
RTLE	.90	66	.06	.11

Note. Small effect for whole sample, LTLE, and RTLE.

In summary, there was no significant relationship between hemispheric dominance for language and the crowding pattern

Hypothesis II

A chi-square, a *t*-test, and a logistic regression were used to assess the second hypothesis. Of the 125 subjects who were typically organized, 15 (10.3% of the total sample) subjects demonstrated high cognitive reserve and 110 (75.9% of the total sample) did not demonstrate high cognitive reserve. Of the 20 subjects who were atypically organized, 1 (0.7% of the total sample) demonstrated high cognitive reserve and 19 (13.1% of the total sample) did not demonstrate high cognitive reserve. Of the 90 LTLE subjects, 74 (82.2%) were typically organized and 16 (17.8%) were atypically organized. Of the 74 LTLE subjects who were typically organized, 10 (11.1%) demonstrated high cognitive reserve and 64 (71.1%) did not demonstrate high cognitive reserve. Of the 55 RTLE subjects, 51 (92.7%) were typically organized and 4 (7.3%) were atypically organized. Of the 51 RTLE subjects who were typically organized, 5 (9.1%) demonstrated high cognitive reserve and 46 (83.6%) subjects did not. Of the RTLE subjects who were atypically organized, none of the subjects demonstrated high cognitive reserve and 4 (7.3%) did not demonstrate high cognitive reserve. The results of the chi-square analysis were insignificant, $X^2 = .473$. Results are displayed in Table 4.

The results of the *t*-tests were insignificant for the whole sample $t(143) = .58$, $p > .005$, the LTLE patients $t(88) = .59$, $p > .005$, and the RTLE patients $t(53) = .99$, $p > .005$. Results displayed in Table 5.

Table 4

Chi-Square Outcome for Hemispheric Dominance and Cognitive Reserve

		Reserve	No Reserve	Total
RTLE				
	Typical	5	46	51
	Atypical	0	4	4
	Total	5	50	55
LTLE				
	Typical	10	64	74
	Atypical	1	15	16
	Total	11	79	90
Total				
	Typical	15	110	125
	Atypical	1	19	20
	Total	16	129	145

Note. Total n = 145 was less than the overall n due to missing data. RTLE = right temporal lobe epilepsy. LTLE = left temporal lobe epilepsy.

Table 5

T-test Outcome for Hemispheric Dominance and Cognitive Reserve

	t	df	p	*Effect Size*
Whole Sample	2.34	143	.58	.19
LTLE	1.93	88	.59	.2
RTLE	1.23	53	.99	.17

Note. Small effect size for whole sample, LTLE, and RTLE.

The result of the logistic regression for the whole sample was insignificant at an $\alpha = .005$ level, ($p = .03$). Additional analyses were conducted to further understand this question. The result of the logistic regression for the LTLE patients was insignificant at an $\alpha = .005$ level, ($p = .11$), and the result of the logistic regression for the RTLE sample was insignificant at an $\alpha = .005$ level, ($p = .36$). Results displayed in Table 6.

In summary, there was not a significant relationship between hemispheric dominance for language and cognitive reserve or the interaction between cognitive reserve and crowding and hemispheric dominance for language in the whole sample, LTLE sample, or RTLE sample.

Hypothesis III

A discriminant function analysis was conducted to test the third hypothesis. Due to the small sample size (Typical = 116; Atypical = 18), results are reported with caution. The overall result was not significant, $p = .124$. Results displayed in Table 7**.** In summary, the neuropsychological variables were not able to predict hemispheric dominance for language.

Table 6

Regression Model Summary for Independent Variables and Hemispheric Dominance for Language

	B	SE	Wald	X^2	df	*p*
Constant	-1.85	.247	56.28		1	.000
Side TLE				2.64	1	.104
Cognitive Reserve				6.37	1	.012*
Crowding				.19	1	.660
Overall				8.91	3	.03*

Note. * $p < .05$ but above cutoff of $p < .005$

Table 7

Discriminant Function Summary for Independent Variables and Hemispheric Dominance for Language

	Wilks Lambda	X^2	df	*p*
Overall	.81	26.22	19	.124

Chapter 6: Discussion

The goals of the present study were to determine the prevalence of the crowding pattern and the prevalence of cognitive reserve in typically organized and atypically organized patients with TLE, as well as to determine whether neuropsychological test data would predict hemispheric dominance for language in patients with TLE. One of the primary roles of the neuropsychologist in the presurgical evaluation for patients with TLE is to identify the potential risk to cognitive functioning as a result of the surgery in comparison to the risk of cognitive decline due to TLE without the surgery (Arora et al., 2009; Drane et al., 2012). Research has shown variability in patterns on neuropsychological test data in patients with TLE (Gargo et al., 2013; Wang et al., 2011). To accurately inform patients of the risk to cognition, more research is needed on the neuropsychological profiles of patients with TLE and factors contributing to the varying patterns. This study sought to fill this void.

Crowding in Temporal Lobe Epilepsy Patients

The researcher expected to find relatively low rates of the crowding pattern in the sample, suggesting the pattern occurs for only a subset of individuals. As expected, of the 115 LTLE subjects, 12 demonstrated the crowding pattern. This is not surprising, because it is a rare phenomenon within the literature, though small sample sizes are a limitation of prior studies on the topic (Satz et al., 1994; Strauss et al., 1990). The RTLE subjects were not coded for the binary crowding score, because that would be the expected pattern based on the lesion location and, therefore, that pattern would not be explainable by the mechanism of crowding.

It was hypothesized that the prevalence of patients with temporal lobe epilepsy who demonstrate the crowding pattern on neuropsychological test data would be higher in the atypical hemispheric dominance group than in patients from the typical hemispheric dominance group. The chi-square analysis and the *t*-test of crowding and hemispheric dominance were insignificant and do not suggest a relationship between crowding and atypical hemispheric dominance; however, the results of the chi-square analysis were likely impacted by the small sample size, with some cells in the chi-square under the minimum requirement of 5 subjects per cell. As an alternative means of testing this hypothesis, *t*-tests were conducted on the whole sample and in the LTLE and RTLE samples. Similarly, the analyses were likely impacted by the small number of atypical patients. Therefore, the hypothesis was not supported during statistical analysis and crowding was not predictive of atypical hemispheric dominance for language in TLE patients.

Interestingly, crowding was not related to atypical hemispheric dominance for language. This result is surprising because the crowding hypothesis is a behavioral observation of the sparing of language functions and impairment of visuospatial functions in the presence of a left temporal hemisphere lesion, and this pattern could be explained by the dominant hemisphere for language being the opposite hemisphere of the lesion location (Satz et al., 1994; Strauss et al., 1990). It is possible that patients who are atypically organized preserve some language functioning but not enough to be defined as intact by clinical standards. It is also possible that patients who are atypically organized show intact language and a decline in other skills but not to the extent that would warrant clinical impairment, or that patients who are atypically organized demonstrate a diffuse pattern of impairments when compared to their counterparts. The atypical hemispheric dominance group consisted of patients with right or bilateral hemispheric dominance. It is possible that including patients with bilateral hemispheric dominance for language influenced the overall rates of crowding, and that there are higher rates of crowding in patients with greater right hemispheric dominance for language. Finally, atypicality was a binary variable. Using a continuous variable, assessing amount of atypicality may have been a more sensitive measure with higher rates of atypicality associated with higher rates of crowding.

Cognitive Reserve in Temporal Lobe Epilepsy Patients

It was hypothesized that the prevalence of cognitive reserve in patients with temporal lobe epilepsy in the atypical hemispheric dominance group would be different than in patients from the typical hemispheric dominance group. This was not supported by statistical analyses. There was no significant difference between the typical and atypical groups in the chi-square analysis or on the *t*-tests. The interaction between crowding and cognitive reserve was insignificant in the logistic regression on the whole sample, RTLE sample, or LTLE sample.

There are a variety of reasons for the null findings. First, the small sample size in some of the cells of the chi-square analysis likely influenced the ability of the test to detect a difference if one exists. Second, the index score developed as a continuous variable for crowding for use in the logistic regression takes into consideration the amount of discrepancy between visual spatial skills and verbal skills estimates, whereas the binary estimate does not take into account this discrepancy. Third, RTLE patients were not coded as demonstrating a crowding pattern for the chi-square analysis, as this is the expected pattern for RTLE patients based on the lesion location, but they were included in the logistic regression. Although they were included in the logistic regression analysis, side of temporal lobe epilepsy was also included as an independent variable to control for its influence. To further understand this relationship, a logistic regression was run in the LTLE sample and RTLE sample. The interaction between crowding and cognitive reserve was not significant in the RTLE or LTLE samples. This may be because the sample size was too small to detect a difference if one exists. It also may be because the power for the logistic regression was low, also making it difficult to detect a difference if one exists.

The results of this study are surprising because cognitive reserve has been used to explain the preservation of cognitive functioning in the face of illness or injury (Akman et al., 2003). The predictive power of cognitive reserve could be explained with higher rates for either the typical or atypical group. Higher rates of cognitive reserve could be explained in patients with typical hemispheric dominance because those with higher cognitive reserve are able to sustain a greater injury prior to needing to shift language to the other hemisphere; however, higher rates of cognitive reserve could be explained in patients with atypical hemispheric dominance because those with higher cognitive reserve have more underlying neuronal networks, including those connecting to the alternate hemisphere. Furthermore, because cognitive functions rarely operate in isolation, patients with higher reserve may perform better on neuropsychological testing because they are able to use other cognitive domains (e.g. attention, executive functioning) to compensate for deficits.

Predictive Value of Neuropsychological Data

It was hypothesized that neuropsychological testing can predict hemispheric dominance for language in the context of unilateral temporal lobe epilepsy. This hypothesis was not supported during statistical analysis. No distinct pattern could differentiate between typically and atypically organized patients on the 17 neuropsychological, cognitive reserve, and temporal lobe side variables used in this study. The outcome was likely impacted by the small sample size and the variability of the assessments used with this sample.

This finding was surprising because it was expected that atypically organized patients would demonstrate a pattern unique to this subgroup. Nevertheless, research has suggested that as there are four atypical memory profiles possible, and as many as 75% of patients with MTLE with HS had atypical memory profiles (Gargo et al., 2013). Other studies have found more diffuse profiles with impairment in more than one cognitive domain (Wang et al., 2011). The lack of a distinct pattern may have occurred because the atypical hemispheric dominance group has a more diffuse pattern or because of additional factors influencing the neuropsychological pattern, such as antiepileptic medications. Prior research found that age of onset was the greatest predictor of IQ; duration of epilepsy had the greatest effect on the WCST score; seizure frequency was the strongest predictor of semantic memory, episodic memory, and language impairments; and number of antiepileptic medications was the greatest predictor of processing speed and working memory impairments (Wang et al., 2011). This research suggests that these factors should be controlled for in order to truly understand the pattern of atypically organized temporal lobe epilepsy patients on neuropsychological test data.

Finally, the lack of a distinct pattern also may have occurred because the atypical group is comprised of patients who demonstrated right hemispheric dominance for language but also bilateral hemispheric dominance for language. Because patients who demonstrated bilateral hemispheric dominance were included in the atypical group, the neuropsychological profiles are likely to be more diverse with varying degrees of impairment on different measures.

Group Differences Between Typically and Atypically Organized Subjects

Atypically organized subjects were more likely to be left-handed than typically organized subjects, particularly for the subjects with RTLE. Atypically organized subjects were slightly older than the typically organized subjects at the time of testing. LTLE subjects who were atypically organized were slightly more likely to be male than female, but rates were comparable for RTLE subjects. Rates of typicality for fMRI and the Wada test were comparable. Surprisingly, age of seizure onset was comparable, but approximately 1 year older for atypical subjects than typical subjects. Also unexpectedly, total years of education were comparable between the typical and atypical subjects. The higher rates of age of seizure onset for the atypical rates may be explained by the exclusionary criteria. Prior research has found that subject with early age of seizure onset who were atypically organized were more likely to have a lower IQ (Wang et al., 2011). As such, these subjects may be underrepresented in my sample.

Implications

The primary implication of the present study is that although atypical hemispheric dominance for language is greater in patients with TLE, it is still a rare phenomenon. The effect of TLE on cognitive functioning is influenced by a variety of factors, including age of onset, frequency of seizures, seizure duration, and antiepileptic medications (Akman et al., 2003; Dabbs et al., 2012; Hermann et al., 2010; Pai & Tsai, 2005). Because atypical hemispheric dominance is rare and because of the multifactorial nature of temporal lobe epilepsy on cognitive functioning, a larger sample size is needed to understand the factors influencing the higher rates of atypical hemispheric dominance for language in this population.

It is also possible that the shift from typical to atypical hemispheric dominance for language represents the attempt of the brain to optimize cognitive functioning rather than sacrifice one cognitive function for another. As such, it may be expected that there would be a more diffuse pattern of decline rather than specific cognitive deficits. The behavioral observation of “relative” sparing of language functions may still result in clinical impairment on neuropsychological testing, with less functional, adaptive impairment.

A second implication of the present study is that patients with temporal lobe epilepsy would benefit from an "intellectually enriching lifestyle" as a means of supporting cognition, promoting neurogenesis, and reducing the severity of impairments (Akman et al., 2003; Ruan et al., 2014; Stern, 2009; Sumowski & Leavitt, 2013). Engaging patients in activities that have been shown to increase cognitive reserve can serve as a protective factor against cognitive decline. There may be a variety of challenges to engagement in certain activities, including the risk of seizures and injury during some physical activities or the effect of poorly controlled epilepsy on psychological and social functioning. Nevertheless, encouraging patients to engage in safe activities can serve as an important protective factor.

Limitations to the Current Study

There are a number of limitations to this study. The researcher used an archival data set, which was collected over a long length of time. Because of this, the battery of neuropsychological tests was updated with current editions of the tests. These tests have strong correlations with each other but resulted in the use of the normed scores rather than the raw scores. The battery was also updated in efforts to include the most accurate assessments for the sample. Because of this, the subtest used to assess visuospatial memory varied over time and, as such, different subjects had different visuospatial memory tests used to assess this construct. The subtests were highly correlated, but it is possible that this affected the outcome.

Atypical hemispheric dominance for language is a rare phenomenon and although the rates are higher in patients with TLE, the number of subjects who were atypically organized was small (n = 23). The small sample size likely impacted the ability to detect an effect if one exists. For the chi-square analyses, there are cells that had less than the recommended five subjects, making a statistically different effect difficult to detect. In discriminant function analysis, it is recommended that there are 20 subjects for each predictor variable (Sheskin, 2007). There were 18 predictor variables used in the discriminant function analyses (17 neuropsychological variables and 1 temporal side). The sample size was not large enough to meet the recommendation for the number of predictor variables, making it difficult to detect an effect if one exists. Additionally, the atypically organized group was comprised of patients with both right and bilateral hemispheric dominance. This also likely impacted the ability to detect distinct patterns on neuropsychological data.

Similar to other studies on cognitive reserve, a limitation of this study was the operational definition of cognitive reserve. Premorbid IQ was used as a proxy for cognitive reserve. Cognitive reserve is the extent to which the brain has resilient and restorative factors due to latent connectivity in the brain that is utilized as a result of injury or disease. To truly measure cognitive reserve, it would be necessary to utilize a measure that captures connectivity in the brain, which is out of the scope of this paper.

There are also a number of potential confounding variables, including age of onset, antiepileptic medications, seizure frequency, duration of epilepsy, and other illnesses or health concerns that could impact cognition. Due to the small sample size of the subjects with atypical hemispheric dominance, variability of neuropsychological test data, and number of extraneous variables, the subjects were unable to be matched on all variables. As such, it is possible that these factors could have influenced cognitive reserve or patterns seen on neuropsychological test data. Furthermore, socioeconomic status (SES) has the potential to impact cognitive reserve, but it also has the potential to impact access to healthcare. It is possible that higher cognitive reserve may be due to better access to healthcare or the interplay between the two variables.

Because the sample focused on patients with unilateral temporal lobe epilepsy, it is unknown whether the results can generalize to patients with other forms of epilepsy, such as frontal or extratemporal lobe epilepsy. Further, it is unknown to what extent the results can generalize to children with epilepsy.

Suggestions for Future Research

A prospective study would be optimal for conducting this research; however, this may be unrealistic due to the nature of the study and the ability to acquire a sufficient sample. Future research should utilize a larger sample size and examine the same neuropsychological test variables. Furthermore, future research should use an operational definition of cognitive reserve that incorporates neuronal connectivity. Additionally, future research should study the different subgroups within the TLE group to determine the underlying factors that result in the groups, as well as the treatment outcomes for each group.

Future research may also benefit from examining the LTLE sample and RTLE sample as two distinct groups. If the transition of language from the left to the right hemisphere represents the attempt of the brain to optimize functioning, it would be interesting to see whether an inverse crowding pattern (spared visual spatial functions but impaired language functions) is present in RTLE patients. If the mechanism is due to the effort of the brain to optimize all cognitive functions, then it is reasonable to expect this pattern in a sample of patients with right hemisphere lesions. Finally, future research should quantify the amount of atypical hemispheric dominance and determine whether there is a difference between groups with more or less atypicality on hemispheric dominance for language.

General Discussion

There are multiple benefits to this study, including making appropriate treatment recommendations and spurring future treatment research. The results of this study suggest neuropsychological data were unable to predict hemispheric dominance for language in TLE patients and alternative tests (e.g. fMRI and/or Wada) should continue to be used to determine hemispheric dominance for language, and that insurance companies should provide coverage as it is clinically indicated. Although there was not a significant relationship between hemispheric dominance for language and cognitive reserve, patients with temporal lobe epilepsy may still benefit from those factors that constitute "an intellectually enriching lifestyle."

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